

## 《研究速報》

# Dipyridamole-Loading Myocardial Imaging with Thallium: Basic Investigation of its Usefulness

Michihiro NARITA\*, Tadashi KURIHARA\*, Masahisa USAMI\*, Minoru HONDA\*\*,  
Tadashi OGAWA\*\*, Keisuke KANAO\*\*, Shoso NEZUO\*\*\*  
and Toshitami SAWAYAMA\*\*\*

Exercise stress myocardial imaging with thallium-201 (Tl) has been used as a useful noninvasive method for the detection of coronary artery disease (CAD), but its diagnostic accuracy was restricted within the limits of around 75%<sup>1,2)</sup>. Recently, Gould et al<sup>3)</sup> reported the validity of dipyridamole-loading myocardial imaging to detect CAD and its possibility to supplement the diagnostic accuracy of the exercise stress myocardial imaging. But little is known about the effect of dipyridamole on myocardial Tl uptake especially in the presence of coronary stenosis. Therefore, we have studied the effect of dipyridamole on myocardial blood flow (MBF) and myocardial Tl concentration by coronary artery occluded dogs to clarify the usefulness of dipyridamole-loading myocardial imaging. We also studied the effect of dipyridamole on Tl concentration in organs adjacent to the heart.

## Methods

The 20 adult mongrel dogs (10–16 kg) were anesthetized with sodium pentobarbital (30 mg/kg) and ventilated with a Harvard respirator. After a left thoracotomy, a polyvinyl tube was inserted into the left atrium for the administration of microspheres<sup>4)</sup>.

In 15 dogs, left anterior descending coronary artery (LAD) was ligated at its middle portion.

\* Department of Internal Medicine, Sumitomo Hospital

\*\* Division of Nuclear Medicine, Sumitomo Hospital

\*\*\* Department of Cardiology, Kawasaki Medical College

受付: 55年6月2日

最終稿受付: 55年8月4日

別刷請求先: 大阪市北区中之島 5-2-2 (☎ 530)

住友病院内科

成田 充 啓

Forty-five minutes after the ligation, in 5 dogs (dipyridamole-group), dipyridamole (0.57 mg/kg) was injected intravenously and 5 minutes later Tc-99m-albumin-microspheres (15  $\mu$ m in diameter) were injected into the left atrium, and Tl (1 mCi) was injected intravenously. In the remaining 10 dogs (control-group), Tc-microspheres and Tl were administered after LAD ligation without dipyridamole-loading.

In the other 5 dogs, LAD was partially occluded at its middle portion by using a half cylindrical tube (0.5 cm in length). About 30 minutes later, Tc-microspheres were injected into the left atrium. Then, dipyridamole (0.57 mg/kg) was injected intravenously, and 5 minutes later, microspheres labeled with indium-111 were administered into the left atrium, while Tl was administered intravenously. The degree of the coronary stenosis was confirmed by coronary angiography.

About 20 minutes after Tl administration, the left ventricle was divided into 64 segments<sup>4)</sup>. Left ventricular, right ventricular, lung and liver samples were counted in a gamma well counter. A distribution of isotope in each sample was expressed as a ratio of radioactivity of each sample to the total injected radioactivity (% injected dose/g-tissue)<sup>4)</sup>.

## Results

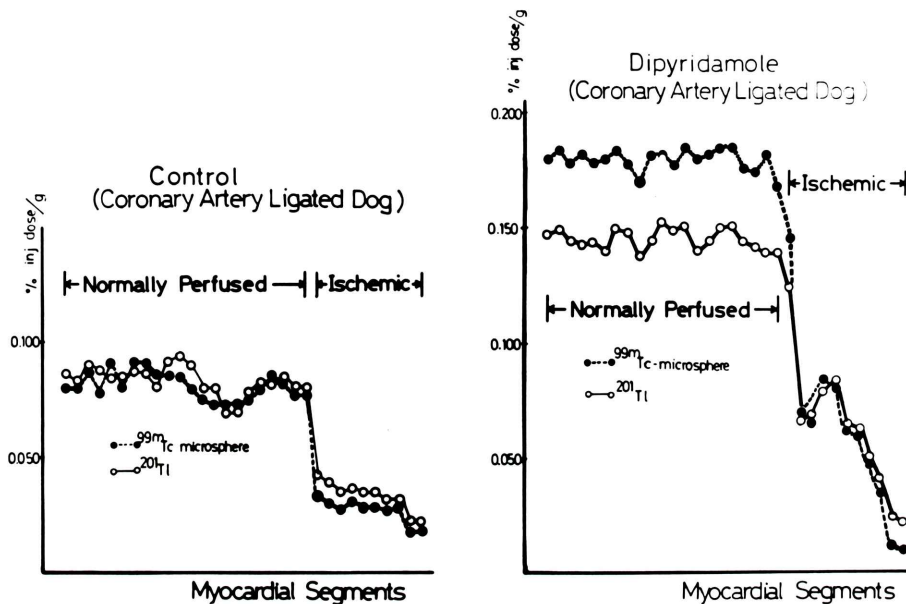
**Dogs with Coronary Artery Ligation** In control-group, coronary artery ligation caused significant changes in heart rate (HR) (Mean  $\pm$  SD;  $136.5 \pm 7.9 \rightarrow 155.0 \pm 6.2$  beats/min.,  $p < 0.01$ ) and mean aortic pressure (mean AP) ( $102.5 \pm 8.7 \rightarrow 90.0 \pm 10.8$  mmHg,  $p < 0.01$ ). But these values were remained stable after the coronary artery ligation. In dipyridamole-group, coronary artery ligation caused significant changes in HR ( $134.5 \pm 8.0 \rightarrow 150.0 \pm 8.2$  beats/min.,  $p < 0.01$ ) and mean AP

( $134.2 \pm 8.0 \rightarrow 94.0 \pm 8.8$  mmHg,  $p < 0.01$ ) as same degree as the control dogs. In this group, following dipyridamole administration, mean AP decreased significantly ( $94.0 \pm 8.8 \rightarrow 80.8 \pm 10.5$  mmHg,  $p < 0.01$ ) but HR decreased insignificantly ( $150.0 \pm 8.2 \rightarrow 140.5 \pm 10.2$  beats/min., NS).

In control-group, MBF (microsphere concentra-

tion) and the myocardial TI concentration coincided well as shown in Fig. 1 (left hand), and the mean correlation coefficient was  $0.927 \pm 0.008$ .

In normally perfused segments, dipyridamole increased MBF on an average of 142% over control value ( $0.085 \pm 0.012 \rightarrow 0.206 \pm 0.025\%$  injected dose/g-LV). In the mean time, dipyridamole in-



**Fig. 1** Left-hand: The relationship of myocardial Tc-microsphere concentration (MBF) to TI concentration in one of coronary artery ligated control dogs. They coincided well in normally perfused and ischemic segments.

Right-hand: The effect of dipyridamole on myocardial Tc-microsphere concentration (MBF) and myocardial TI concentration in one of coronary artery ligated dogs. Dipyridamole increased both Tc-microsphere concentration and TI concentration in normally perfused myocardial segments. But the increment of microsphere concentration was larger than that of TI concentration.

**Table 1** Effects of dipyridamole on TI concentration in heart, liver and lung

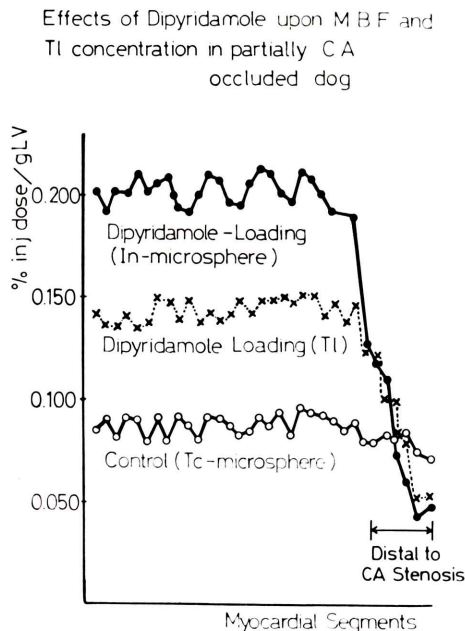
Sample	Control	Dipyridamole	
	% inj. dose/g (mean $\pm$ SD)	% inj. dose/g (mean $\pm$ SD)	Percentage change
Left Ventricle (normally perfused)	$0.088 \pm 0.011$	$0.143 \pm 0.020^*$	+62%
Left Ventricle (ischemia by CA ligation)	$0.034 \pm 0.108$	$0.044 \pm 0.029$	+29%
Right Ventricle	$0.047 \pm 0.010$	$0.096 \pm 0.019^*$	+104%
Lung	$0.050 \pm 0.012$	$0.073 \pm 0.015^*$	+46%
Liver	$0.040 \pm 0.010$	$0.063 \pm 0.012^*$	+58%

\* $p < 0.01$  CA: Coronary Artery

creased the myocardial Tl concentration on an average of 62% over control value (Fig. 1, Table 1). Although the increment of myocardial Tl concentration following dipyridamole in normally perfused segments was less than that of MBF, differences in myocardial Tl concentration between normal and ischemic segments were augmented.

Dipyridamole also augmented right ventricular, hepatic and pulmonary Tl concentration in the different degree (Table 1).

**Dogs with Partial Coronary Occlusion** In 5 dogs, we made partial coronary occlusion of 25%, 60% (2 dogs), 75% and 80% respectively. In every case, HR and mean AP did not change following partial occlusion, but dipyridamole caused decrease in HR ( $135.4 \pm 11.3 \rightarrow 127.0 \pm 10.5$  beats/min. NS) and mean AP ( $114.2 \pm 4.8 \rightarrow 97.8 \pm 10.5$  mmHg,  $p < 0.01$ ). In all dogs, left ventricular MBF was maintained homogeneously after partial occlusion.



**Fig. 2** The effect of dipyridamole on myocardial blood flow and myocardial Tl concentration in a dog with 80% of coronary artery stenosis. Myocardial blood flow was maintained homogeneous before dipyridamole administration. But dipyridamole developed ischemia and low Tl concentration distal to the stenosis.

But, in cases with greater than 60% of coronary stenosis, dipyridamole caused nonhomogeneity of MBF and Tl concentration, in the post-stenotic segments, Tl concentration was less than 50% of normally perfused myocardial segments (Fig. 2). Besides, unhomogeneity of Tl concentration increased parallel to the degree of coronary stenosis.

### Discussion

Previous animal experiments showed that dipyridamole induced coronary vasodilatation could provoke nonhomogeneity of MBF distal to the subcritical stenotic segments<sup>5</sup>). Gould et al<sup>3</sup>) performed dipyridamole-loading myocardial imaging to detect CAD. But we can not extend the MBF changes induced with dipyridamole straightforwardly to myocardial imaging with Tl, because myocardial Tl uptake is not proportional to flow if the increase in coronary flow is induced without elevating myocardial oxygen demand<sup>6</sup>). In our animal experiments, dipyridamole did not increase myocardial Tl concentration so much as MBF in normally perfused myocardium, but the drug apparently augmented the differences of Tl concentration between the normally perfused and ischemic segments. In dogs with greater than 60% of coronary stenosis, dipyridamole induced nonhomogeneity in Tl concentration as well as MBF unbalance distal to the post-stenotic myocardium. These facts indicated the usefulness of dipyridamole-loading myocardial imaging to detect subcritical stenosis. But in the clinical practice, especially in the longstanding CAD, the effect of dipyridamole on collateral circulations (coronary steal), as well as the degree of coronary stenosis, might have an important role to develop Tl uptake nonhomogeneity in cases with subcritical stenosis<sup>7</sup>). And we are going to study the effect of dipyridamole on myocardial Tl uptake in dogs with chronically obstructed coronary artery.

### References

- 1) Ritchie JE, Zaret BL, Strauss HW et al: Myocardial imaging with thallium-201: A multicenter study in patients with angina pectoris or acute myocardial infarction. *Am J Cardiol*, **42**: 345-350, 1978
- 2) Narita M, Usami M, Kurihara T: Exercise stress myocardial perfusion scintigraphy with thallium-



201. Jpn Cir J, **43**: 191-204, 1979
- 3) Gould KL, Wescott RJ, Albro PC et al: Noninvasive assessment of coronary stenoses by myocardial imaging during pharmacologic coronary vasodilatation. Am J Cardiol, **41**: 279-287, 1978
- 4) Narita M, Kurihara T, Usami M et al: Quantitative assessment of myocardial imaging with thallium-201, basic study and its clinical applications. Jpn J Nucl Med, **16**: 897-905, 1979
- 5) Flammeng W, Wüsten B, Schaper W: On the distribution of myocardial flow: Effects of arterial stenosis and vasodilatation. Basic Res Cardiol, **64**: 435-446, 1974
- 6) Weich HF, Strauss HW, Pitt B: The extraction of thallium-201 by the myocardium. Circulation, **56**: 188-191, 1977
- 7) Becker LC: Conditions for vasodilator-induced coronary steal in experimental myocardial ischemia. Circulation, **57**: 1103-1110, 1978

## 要 旨

成田 充啓\* 栗原 正\* 宇佐美暢久\* 本田 稔\*\*  
小川 正\*\* 金尾 啓右\*\* 鼠尾 祥三\*\*\* 沢山 俊民\*\*\*

\*住友病院内科, \*\*住友病院アイソトープ室, \*\*\*川崎医科大学循環器内科

Dipyridamole 負荷 Tl 心筋シンチの有効性を検討するため、冠動脈結紮犬(15頭)、冠動脈狭窄犬(5頭)を用い、dipyridamole の局所心筋血流量、心筋内 Tl 濃度に及ぼす影響を検討した。

冠動脈結紮犬の内対象群では、局所心筋血流量と心筋内 Tl 濃度はよく一致した( $r=0.927 \pm 0.08$ )。Dipyridamole 群では、dipyridamole は、健常部の心筋血流量を 142% 増加したが、心筋内 Tl 濃度の増加は 62% にすぎなかった。しかし健常部と虚血部の Tl 濃度差は dipyridamole により大と

なった。また冠動脈狭窄犬では、60%以上の狭窄を有する例で、dipyridamole 投与により、狭窄末梢部で心筋血流量、心筋内 Tl 濃度の不均衡を招来した。かつ、狭窄末梢部での心筋内 Tl 濃度は健常部の50%以下であった。またこの不均一の度合は、冠動脈狭窄の程度に平行していた。以上の結果は、冠動脈疾患診断における dipyridamole 負荷シンチの有用性を示唆した。

**Key words:** Thallium-201, Dipyridamole, Myocardial Blood Flow